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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/837,459	04/18/97	MCKEE M	4995.0023

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EXAMINER	
PORTNER, V	
ART UNIT	**PAPER NUMBER**
1641	24

DATE MAILED: 03/30/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/837,459	McKee et al
Examiner	**Group Art Unit**
Portner	1641

☒ Responsive to communication(s) filed on *Feb 4, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *60* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *60* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 1-27, 33-50, 56-59, 62-63 have been canceled and only claim 60 is pending.

Please Note: The recitation of "intimin" in the claims is being read in light of the definition set forth in the instant specification to include intimin, intimin-like proteins and invasin proteins.

Claim Rejections - 35 U.S.C. § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 60 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the production of antibodies to intimin and screening for antibodies with blocking ability in an in vitro assay method, as well as teaches the administration of antibody compositions to provide an immune effect the instantly claimed invention, does not reasonably provide enablement for the administration of any anti-intimin antibody composition to any epitope in any location of intimin in order to obtain a passive immune protective effect. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

The prior art of record teaches (deAzavedo) that the C-terminal region of the attaching and effacing protein of EHEC is key to the process of binding to host patient receptors to cause

infection and teaches that this domain carries the epitopes recognized by neutralizing monoclonal antibodies. As the antibodies recited in claim 60 may be any type of anti-intimin antibody, to include: monoclonal, monospecific, chimeric, polyclonal, bifunctional, Fab fragements, the portion of intimin to which the antibodies bind would need to be clearly set forth inorder to obtain the desired protective effect of preventing infection through blocking (either partial or complete blocking) of receptor association. Chart et al(1988) have shown that some serum I.G. does not inhibit adherence of EPEC to Hep-2 cells and it is therefore possible that the type of immune response required in vivo is a specific type of mucosal immunity, wherein Cravioto et al showed that secretory IgA provided protection against infection when administered to a patient in human breast milk and blocked the adherence of human EPEC. It would require undue experimentation by the person of skill in the art to use any antibody of any binding specificity, to any epitope of intimin, by any mode of administration of any amount of anti-intimin antibodies to produce a passive protective immune response. No working examples are presented with the missing information. Therefore, the person of skill in the art could not make and use the claimed invention commensurate in scope as now claimed.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 60 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The method is incomplete as no correlation step is recited to define that the amount of anti-intimin antibodies administered actually provided for a passive immune protective effect. Any amount of anti-intimin antibodies may be administered and the effect resultant from this administration is not correlated with the preamble of the claim and therefore does not distinctly claim Applicant's invention.

Claim Rejections - 35 U.S.C. § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 60 is rejected under 35 U.S.C. 102(b) as being anticipated by Cravioto et al (1991).

Cravioto et al disclose a method of administering secretory IgA to a patient, wherein the patient is an infant in need of immunological protection against infection. The method encompasses administration of human breast milk and colostrum which comprises antibodies to enteropathogenic Escherichia coli antigen of 94 kDa that was a plasmid associated virulence factor (see page 1251, col. 2, paragraph 1; see figure 6, page 1251, col. 2 and figure 3, page

1251, bottom of page). The reference states the "[O]ligossacharides and sIgA could represent two of the most important protective fractions during the first weeks of lactation. Page 1253, col. 2, paragraph 2" and teaches the importance of immunoglobulins as a "[v]ehicle for protection against enteric infection in infants born in developing countries." The reference inherently teaches the claimed method, wherein the antibodies administered were in human breast milk administered to an infant which is immunologically not mature and in need of passive immune protection against infection in the first weeks of life. If applicants contend that this is not the case, applicants are advised that the Office does not have the facilities for examining and comparing applicant's product with the prior art, and that the burden is on applicant to show a novel or unobvious difference between the claimed method and the method of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. and Int.)

7. Claim 60 is rejected under 35 U.S.C. 102(b) as being anticipated by Ashkenazi et al (1988) in light of Agin et al.

Ashkenazi et al disclose that intravenously administered immune globulin provided a beneficial effect in a few children with hemolytic uremic syndrome to in a method of providing passive immune protection. The antibodies administered were commercially available vaccine compositions which contained neutralizing antibodies and inherently comprised antibodies to

intimin because protective intimin antibodies have been shown to be pre-existing in serum (Agin) and would therefore be present in the compositions of Ashkenazi. The method of Ashkenazi anticipates the now claimed method.

Claim Rejections - 35 U.S.C. § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Isberg et al (US Pat.5,310,654). Please Note: The following rejection is being made because anti-Invasin antibodies, as defined in the instant specification falls within the definition of intimin antibodies.

Isberg et al teach and suggest a method of producing and using antibodies to an intimin like protein associated with invasion of Yersinia (col. 7, lines 11-26 and col. 22, lines 20-25) for inhibiting invasion of pathogens in a mammalian host patient. Preparation of antisera for passive immunization is polyclonal in nature and may be isolated and purified from serum by ammonium sulfate precipitation and fractionation according to known techniques. Administration to a mammalian host will generally be in amounts of 50 to 500 mg/kg of host in any physiologically acceptable carrier. Administration will usually be by injection, e.g., intravenously.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to administer anti-intimin antibodies of Isberg to a patient in need thereof because Isberg teaches intimin (invasin) is associated with invasion of the mammalian pathogen Yersinia and blocking of the invasion associated bacterial receptor would inhibit invasion of the pathogen into mammalian host cells and prevent infection and disease. The person of ordinary skill in the art would have been motivated by the reasonable expectation of success of providing a passive immune protection to a patient through administering anti-intimin antibodies (invasin) because blocking of invasion receptors would inhibit the pathogen from infecting a mammalian host cells. In the absence of a showing of unexpected results, the cited reference obviates the now claimed invention.

10. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pace et al (US Pat.5,681,736). Please Note: The following rejection is being made because anti-invasion plasmid antigen (Ipa, col. 3, lines 19-25 of '736) antibodies, as defined in the instant specification falls within the definition of intimin antibodies.

Pace et al teach and suggest a method of producing and using antibodies to an intimin like protein associated with invasion of Shigella (col. 4, lines 57-59 and col.5, lines 66-67 and col. 6, lines 1-2) for inhibiting invasion of a patient. Preparation of antisera for passive immunization is clearly taught (col. 10, lines 63-67 , col. 11, lines 1-33) and may be isolated and purified

according to known techniques. Administration to a mammalian host will generally be in an effective amount to prevent infection (col. 10, lines 43-58).

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to administer anti-intimin antibodies of Pace et al to a patient in need thereof because Pace et al teach intimin (Ipa) is associated with invasion of the mammalian pathogen Shigella and blocking of the invasion associated bacterial receptor would inhibit invasion of mammalian host cells and subsequent infection and disease. The person of ordinary skill in the art would have been motivated by the reasonable expectation of success of providing a passive immune protection to a patient through administering anti-intimin antibodies (Ipa) because blocking of invasion receptors would inhibit the pathogen from infecting a mammalian host cells. In the absence of a showing of unexpected results, the cited reference obviates the now claimed invention.

Conclusion

This is a non-final rejection. No claims are allowed.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

12. Cirillo et al (1995, abstract) is cited to show antibodies to Yersinia invasin induced by active immunization were protective against infection (page 1002, col. 2, paragraph 3, second half of paragraph).

13.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be changing February 7, 1998. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art 1641.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
March 22, 2000

James C. Housel

JAMES C. HOUSEL 3/27/00
SUPERVISORY PATENT EXAMINER